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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Dahm *et al.*

Serial No.: 09/601,645
Confirmation No.: 7793

Filed: August 4, 2000

For: *METHOD FOR THE QUANTITATIVE DETERMINATION OF TUMOR CELLS IN A BODY FLUID AND TEST KITS SUITABLE THEREOF*

Art Unit: 1655

Examiner: Zitomer, S.

I hereby certify that this paper and the attached papers are being deposited with the United States Postal Service as first class mail in an envelope addressed to:
Commissioner for Patents
Washington, D.C. 20231, on this date.

08/03/01
Date

Stephanie Seidman

ELECTION

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Responsive to the Requirement for Restriction, mailed July 3, 2001, applicant elects, with traverse, group II, claims 20-34, and 62-67, directed to a a method for the quantification of tumor cells in a body fluid.

REMARKS

Any fees that may be due in connection with filing this paper may be charged to Deposit Account No. 50-1213. If a Petition for Extension of time is needed, this paper is to be considered such Petition.

Traverse of finding of lack of unity

The Examiner, recognizing that the rules of unity of invention under PCT Rule 13.1 apply to the instant case, urges that there is a lack of unity because the two groups do not relate to a single inventive concept. This conclusion is based upon the premise that the single general inventive feature between the two group is "mRNA encoding the catalytic subunit of human telomerase." The Examiner urges that this mRNA is known (Genbank) and also urges that the method for quantifying mRNA is known in the art (U.S. Patent No. 5,726,019). Applicant respectfully disagrees.

Claims in group I are directed to methods for quantification of tumor cells in a body fluid by concentrating or depleting tumor cells in a sample of a body fluid;

specifically amplifying mRNA coding for the catalytic subunit of telomerase; and then quantitatively determining the amount of amplified nucleic acid to thereby quantifying tumor cells in a body fluid. Dependent claims specify particulars of the method, including the primers.

Claims in group II are directed to methods for quantification of tumor cells in a body fluid by concentrating or depleting tumor cells in a sample of a body fluid; specifically amplifying mRNA coding for the catalytic subunit of telomerase; and then quantitatively determining the amount of amplified nucleic acid to thereby quantifying tumor cells in a body fluid. Claim 20 is directed to the method of claim 1 and specifies that the cells are concentrated by layering the body fluid onto a cell separation medium and centrifuging the layered fluid and medium. Dependent claims specify particulars, for example, regarding the cell separation medium. Hence group II is directed to the method of group I, and specifies particulars of the method. It is not directed to a method for concentrating tumor cells nor to an apparatus. Group II is directed to a method for quantification of tumor cells. Claim 1 specifies that the tumor cells are concentrated and group II includes some specifics about the step of concentrating.

Claims in group III are directed to specific primers and to a kit containing the primers. Dependent claims in group I, specify that these primers are used for amplification.

Cited art

U.S. Patent No. 5,726,019

This patent describes a method for diagnosing lung neoplasia and is based upon the discovery that a nucleic acid molecule that has as particular mutation is associated with lung neoplasia and that this nucleic acid molecule is present in detectable levels in sputum specimens from patients with lung neoplasia. U.S. Patent No. 5,726,019 does not teach or suggest that the amount of mRNA encoding a catalytic subunit telomerase can be used to quantify tumor cells in a body fluid. U.S. Patent No. 5,726,019 does not teach or suggest anything regarding telomerase or mRNA coding for the catalytic subunit of telomerase.

Therefore it does not anticipate any of the pending claims.

Genbank submission

The Examiner states that the sequence of cDNA from mRNA encoding the catalytic subunit of telomerase is available from Genbank. Even assuming that such sequence is known, the disclosure thereof provides no teaching suggestion that the amount of mRNA present in a body fluid can be used to quantitate tumor cells. Furthermore, the Genbank submission does not teach or suggest the particular primers used in the instant methods or kits.

Therefore it does not anticipate any of the pending claims.

Selby (GB 2 260 811)

Selby is directed to methods for diagnosing malignant tumors in which **total** mRNA is extracted from a sample of body fluid and reverse transcribed into cDNA, which is amplified using **primers** based upon **a tissue-specific gene not normally expressed in the body fluid**, followed by analysis to determine whether such amplified cDNA is present. Selby does not suggest using a gene for amplification that is not tissue specific nor does Selby suggest quantification of tumor cells in a body fluid. Selby, thus teaches using a tissue-specific gene, not a gene that is ubiquitously expressed.

Selby does not suggest using a gene for amplification that is not tissue specific nor does Selby suggest quantification of tumor cells in a body fluid. Selby does not suggest anything about the catalytic subunit of telomerase nor suggest that it can be used for quantification of tumor cells in a sample of body fluid. Selby does not teach or suggest that the amount of the mRNA encoding the catalytic subunit of telomerase can be detected in a body fluid nor that such a amount is related to the number of tumor cells in the fluid. Therefore it does not anticipate any of the pending claims.

Thus, the instant claims are clearly novel and are not taught or suggested by the combination of teachings of the cited references. Furthermore, the instant application teaches that the quantity of mRNA that encodes the catalytic subunit of telomerase correlates with telomerase activity better than the quantity of the RNA component of telomerase (International PCT application No. 97/18322; see,

U.S. application Serial No. 09/068,821). Furthermore, neither reference, singly or in combination teaches or suggests the instantly claimed primers, used in the method and specified in dependent claims, and kits.

Therefore, the claims of groups I-III do not lack unity and are so linked as to form a single inventive concept *i.e.* a method for quantifying tumor cells in a body fluid and primers used in the method. Accordingly, withdrawal of the lack of unity objection and restriction requirement is respectfully requested.

Furthermore, if the claims are divided into these groups, particular groups I and II, applicant ultimately could be granted two patents, one directed to the method for quantifying tumor cells in a body fluid by concentrating or depleting tumor cells in a sample of a body fluid; specifically amplifying mRNA coding for the catalytic subunit of telomerase; and then quantitatively determining the amount of amplified nucleic acid to thereby quantifying tumor cells in a body fluid, and a second patent directed to the same method, but specifying that the cells are concentrated by layering the body fluid onto a cell separation medium and centrifuging the layered fluid and medium. If the second patent, which is directed to claims that are encompassed within the claims the first patent, were to issue first obviousness-type double patenting **could not** be held. See MPEP 806, paragraph 3, which states:

> [w]here inventions are related as disclosed but are not distinct as claimed, restriction is never proper. Since, if restriction is required by the Office double patenting cannot be held, it is imperative the requirement should never be made where related inventions as claimed are not distinct.

See, also MPEP 804.01, which states:

> 35 U.S.C.121, third sentence, provides that wherein the Office requires restriction, the patent of either the parent or any divisional application thereof conforming to the requirement cannot be used as a reference against the other. This apparent nullification of double patenting as ground of rejection or invalidity in such cases imposes a heavy burden on the Office to guard against erroneous requirements for restriction where the claims define essentially the same inventions in different language and which, if acquiesced in, might result in the issuance of several patents for the same invention.

Therefore, withdrawal of the requirement for restriction as between groups I-III, and most particularly, as between groups I and II, is respectfully requested.

* * *

In view of the remarks herein, reconsideration of the requirement for restriction and examination of all claims on the merits are respectfully requested.

Respectfully submitted,
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